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Potential Medication-Related Problems in Older Breast, Colon, and Lung Cancer Patients in the United States

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Abstract

Background—Older adults are often exposed to multiple medications, some of which could be inappropriate or have the potential to interact with each other. Older cancer patients may be at increased risk for medication-related problems due to exposure to cancer-directed treatment.

Methods—We described patterns of potentially inappropriate medication (PIM) use and potential drug-chemotherapy interactions among adults age 66+ years diagnosed with stage I–III breast, stage II–III colon, and stage I–II lung cancer. Within the Surveillance, Epidemiology, and End Results-Medicare database, patients had to have Medicare Part D coverage with 1+ prescription in the diagnosis month and Medicare Parts A/B coverage in the prior 12 months. We estimated monthly prevalence of any and cancer-related PIM from 6 months pre- to 23 months post-cancer diagnosis and 12-month period prevalence of potential drug-chemotherapy interactions.

Results—Overall, 19,318 breast, 7,283 colon, and 7,237 lung cancer patients were evaluated. Monthly PIM prevalence was stable pre-diagnosis (37–40%), but increased in the year following a colon or lung cancer diagnosis, and decreased following a breast cancer diagnosis. Changes in PIM prevalence were driven primarily by cancer-related PIM in patients on chemotherapy. Potential drug-chemotherapy interactions were observed in all cohorts, with prevalent interactions involving hydrochlorothiazide, warfarin, and proton-pump inhibitors.

Conclusions—There was a high burden of potential medication-related problems among older cancer patients; future research to evaluate outcomes of these exposures are warranted.

Impact—Older adults diagnosed with cancer have unique medication management needs. Thus, pharmacy specialists should be integrated into multidisciplinary teams caring for these patients.

Keywords

polypharmacy; clinical oncology; geriatrics; administrative claims; healthcare; comorbidity

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Introduction

As the prevalence of multiple chronic conditions increases with age, older adults (age 65+ years) and their healthcare providers often must manage the use of multiple prescription medications. At the same time, age-related changes in body composition and organ function can alter the way the body processes and reacts to drugs, making older adults more sensitive to both the intended and unintended effects of medications.(1) A recent study reported that nearly 40% of older Americans were taking 5 or more prescription drugs (i.e., polypharmacy) in the prior 30 days.(2) This is concerning given that polypharmacy is associated with an increased risk of drug-drug interactions and adverse drug events (ADEs).(3) In addition, polypharmacy increases the chances that an older adult will be prescribed a potentially inappropriate medication (PIM) – i.e., a drug that has a high risk of an ADE relative to its potential benefit, when safer, more effective and well tolerated options are available.(4, 5) Taken together, exposure to polypharmacy, drug-drug interactions, and PIM have serious consequences for the healthcare system, increasing the use of avoidable healthcare services and costs, but also for older adults, decreasing functional capacity and quality of life.(6–10)

As the proportion of cancer patients diagnosed at age 65 years and older is expected to reach 70% by 2030,(11) medication management among this population is a growing public health concern.(12) Compounding the medication management complexities relevant to all older adults is the fact that older adults with cancer are also exposed to cancer-directed treatments, including chemotherapy, which have the potential to interact with concomitant medications used to manage other acute and chronic conditions.(13) Furthermore, cancer patients also frequently use supportive care medications, some of which are considered PIMs, to manage cancer symptoms (e.g., pain and insomnia) and treatment-related side effects (e.g., nausea and diarrhea). As such, individualized assessment and scrutiny of these medications and their benefit-risk balance, considering life expectancy, cancer aggressiveness, and other co-existing conditions, is necessary to optimize medication use in this unique patient population.

At the population-level, documentation of the prevalence of cancer-related PIM use and drug-drug interactions could help alert oncology providers to these problems and highlight subgroups of patients who have high exposure and for whom targeted intervention and medication reviews may be warranted. To generate such knowledge, we conducted a large, population-based study of older adults newly diagnosed with breast (I–III), colon (stage II–III), and lung (stage I–II) cancer to: (1) describe the monthly prevalence of PIM use from 6 months before through 23 months following cancer diagnosis, with a specific emphasis on cancer-related PIM and (2) quantify the 12-month period prevalence of potential drug interactions among patients treated with specific chemotherapeutic agents.

Materials and Methods

Data source and study population

We drew upon the Surveillance, Epidemiology and End Results program (SEER)-Medicare database,(14) a linkage of cancer registry and Medicare enrollment and claims data. This

linked database includes cancer cases through 2011 and Medicare claims through 2013. Medicare Part A and B claims provide information on diagnoses and procedures in the hospital and outpatient setting and Part D claims provide information on prescription drug dispensing (available from 2007–2012).

For this study, we identified adults aged 66 years and older who were diagnosed with a first, primary cancer of the colon (American Joint Commission on Cancer 6th Edition (AJCC) stage II or III), breast (AJCC stage I–III), or lung (AJCC stage I–II) from 2007–2011. These cancer sites and stages were selected to identify populations that might receive chemotherapy, excluding older adults diagnosed with advanced stage disease, where the risk-benefit assessment of PIM use is less clear. To be included in the study cohort, individuals had to have: (1) at least 12 months of continuous Medicare enrollment in Parts A and B prior to their diagnosis date (set to the first day of the month of diagnosis) to assess relevant comorbid conditions, (2) Medicare Part D (prescription drug) coverage during the month of diagnosis, and (3) at least one prescription medication dispensed in the month of diagnosis. Individuals who were diagnosed at autopsy, did not survive throughout the month of diagnosis, or had a missing month of diagnosis were excluded.

Patient demographic, clinical, and cancer treatment characteristics

Demographic and tumor characteristics were obtained in the month of diagnosis, including age, sex, race (White, Black, Other), marital status (married, single, divorced/widowed/separated), year of diagnosis, and AJCC stage. Using Medicare claims data, we assessed comorbidity using the Charlson Comorbidity Index(15) (categorized as 0, 1, 2+) during the 12-months prior to the month of diagnosis and medication burden using a count of the number of unique prescriptions (generic name level) in the month prior to the month of diagnosis (categorized as 0–2, 3–5, 6–9, 10+). Using the same 12-month period, we estimated each individual's predicted probability of being frail based on an internally(16) and externally(17) validated Medicare claims-based model including 20 unique variables (e.g., diagnosis of weakness, wheelchair claim, home oxygen claim). The resulting predicted probabilities were categorized as 0–<10% (low probability of frailty), 10–<20% (low-intermediate), 20–<50% (intermediate-high), and 50%+ (high). Finally, we constructed a variable for whether an individual underwent surgical resection or received chemotherapy or radiation in the 6-months following diagnosis. In addition, we constructed indicators for the use of specific chemotherapeutic agents in each month from diagnosis through month 11. Codes used to define cancer treatments from Medicare claims are listed in the Supplementary Materials.

Assessment of PIM Use

We identified PIMs according to the 2012 Beers criteria,(4) a medication screening tool developed to help healthcare providers optimize medication use in older adults. The Beers criteria, originally developed in 1991, have been regularly updated by the American Geriatrics Society. The 2012 Beers criteria include 34 drugs to avoid in older adults and 18 drugs that should be avoided as they could exacerbate a coexisting disease (i.e., drug-disease interactions). Prevalence of any PIM dispensing was evaluated monthly, starting 6 months before and going through 23 months following the diagnosis month (month 0). The pre-

cancer diagnosis period (months −6 to −1) was used to establish baseline PIM use patterns prior to a cancer diagnosis and to facilitate comparison with published prevalence estimates of PIM in the general older adult population. We selected the 23 months following the month of cancer diagnosis to evaluate patterns of PIM use during the initial treatment (month 0–11) and continuing (month 12–23) phases of cancer care,(18, 19) as the transitions in PIM prevalence related to cancer treatment were of particular interest. All analyses were anchored at the month of cancer diagnosis (month 0).

Of particular interest were PIMs related to the alleviation of cancer symptoms and treatment-related side effects (referred to as cancer-related PIMs). We specifically examined the broad Beers criteria categories of “Pain” and “Central Nervous System” to identify cancer-related PIMs for pain, anxiety/depression, and insomnia and then identified specific PIMs frequently used to manage nausea, diarrhea, and appetite in cancer patients. For presentation purposes, cancer-related PIM analyses were limited to specific PIMs that had a >1% prevalence in at least one month for at least one cancer site.

To be included in the denominator for a given month, individuals had to have: (1) at least 12 months of continuous Medicare enrollment in Parts A and B prior to the given month of interest, (2) Medicare Part D (prescription drug) coverage during the month, and (3) at least one prescription medication dispensed (or days’ supply carried over) in a given month. Dispensing of a prescription medication was a requirement for an individual to contribute to the denominator, consistent with prior studies,(20–22) as an adult who is not receiving any prescription medications cannot be exposed to a PIM. Because eligibility was determined on a month-by-month basis, the number of individuals contributing to monthly prevalence measures changes over time.

PIMs were identified using Medicare Parts A, B, and D claims as described by Jiron et al. (22) We first used the Anatomical Therapeutic Chemical (ATC) classification system to identify all medications and classes of medications listed as part of the 2012 Beers criteria and then developed a crosswalk of these medications to their specific National Drug Codes (NDCs). For PIMs due to drug-disease interactions, we used International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9) codes to identify specific conditions in the 12-months prior to the given month of interest.

Assessment of drug interactions with chemotherapeutic agents

We identified potential drug-drug interactions involving chemotherapeutics through a review of the literature(13, 23–29) with confirmation by two clinical pharmacists with expertise in oncology and geriatrics. Our review was limited to potential interactions with chemotherapeutic agents used as initial treatment for stage I–III breast, II–III colon, or I–II lung cancer. We again used the ATC classification system to identify all medications included in our review and developed a crosswalk of these medications to their specific NDCs. A clinical pharmacist further classified each potential drug-chemotherapeutic interaction as minor (caution advised), moderate (monitor/modify therapy), or major (avoid/use alternative) using Micromedex® Online (Micromedex, Inc., Ann Arbor, MI, USA).

The 12-month period prevalence of potential drug-chemotherapy interactions was evaluated on the specific chemotherapy agent-level during the initial treatment phase of care (month 0–11). To be included in the denominator for the period prevalence analyses, individuals had to have: (1) continuous Medicare enrollment in Parts A, B, and D (and no managed care coverage) during the entire initial treatment phase and (2) at least one claim for the administration of a specific chemotherapeutic agent of interest in at least one month during this period. To be included in the numerator, patients had to have a prescription claim for a potential interacting drug and overlapping days' supply with the administration of a specific chemotherapeutic agent of interest. For presentation purposes, we restricted our descriptive analyses to specific chemotherapies that had more than 100 patients in the denominator in an attempt to avoid imprecise estimates. All prevalence with a numerator of <11 were suppressed due to SEER-Medicare privacy rules. Specific chemotherapeutics included were 5-fluorouracil (5-FU)/capecitabine (colon), cyclophosphamide (breast), doxorubicin (breast), methotrexate (breast), paclitaxel (breast, lung), carboplatin (lung), cisplatin (lung), etoposide (lung), and gemcitabine (lung). Tamoxifen (breast) was also included in analysis, but is considered endocrine therapy.

Statistical Analysis

We estimated the monthly point prevalence of any PIM among the three cancer cohorts from the 6 months before through the 23 months following the month of cancer diagnosis (month 0). Given the specific interest in the influence of chemotherapy on the use of PIMs as supportive care agents, month-level analyses were stratified by chemotherapy receipt (yes versus no). The monthly prevalence of specific cancer-related PIMs was computed among the three cohorts. Finally, we estimated the 12-month period prevalence of potential drug-chemotherapy interactions during the initial treatment phase, stratifying results by cancer site. All statistical analyses were performed in SAS version 9.4 (Cary, NC). This study was performed after approval by the University of North Carolina at Chapel Hill Institutional Review Board.

Results

Study population

After applying all study inclusion criteria, there were 19,318 stage I–III breast, 7,283 stage II–III colon, and 7,237 stage I–II lung cancer patients included in our baseline cohorts (Supplemental Table 1). Demographic and clinical characteristics of these patients are reported in Table 1. Median age at cancer diagnosis was similar across cohorts at 75 years for breast and lung cancer to 78 years for colon cancer. Variation in the burden of comorbidity at the time of cancer diagnosis was observed across the three cohorts, where lung cancer patients had the highest proportion of patients with a Charlson comorbidity score of 2 or more (lung: 36%, colon: 26%, and breast: 19%) and were dispensed the greatest number of prescription medications in the month prior to cancer diagnosis (% receiving 6+ medications, lung: 33%, colon: 27%, and breast: 25%). However, colon cancer patients had the highest probability of being frail (using a claims-based model), while breast cancer patients had the lowest probability. During the six months following cancer diagnosis, 98% of all colon cancer patients and 94% of breast cancer patients underwent

surgical resection, compared with only 46% of lung cancer patients. Chemotherapy was most common among colon cancer patients (34%), while radiation was frequent among breast cancer patients (44%).

Monthly prevalence of any PIM

The monthly prevalence of any PIM prior to cancer diagnosis was similar across all three cancer cohorts, hovering between 37–40% (Figure 1), similar to general population estimates among Medicare beneficiaries.(22) However, following cancer diagnosis, different patterns emerged. The prevalence of PIM among breast cancer patients consistently decreased over the period following diagnosis, whereas PIM prevalence sharply increased in the first few months following a colon or lung cancer diagnosis, and slowly decreased back to pre-diagnosis levels over the following 23 months. Decreases in PIM prevalence in the breast cancer cohort were attributable to decreased dispensing of estrogen following diagnosis (9% at six months prior to diagnosis to 0.5% one year after diagnosis).

Stratification by chemotherapy receipt

We further plotted the monthly prevalence of any PIM dispensing stratified by chemotherapy receipt (Figures 2a–c). Longitudinal patterns across cancer sites were consistent showing a sharp immediate increase in the monthly prevalence of both PIM dispensing among individuals who initiated chemotherapy within the first six months following cancer diagnosis. In contrast, the monthly prevalence of PIM remained relatively constant among those who do not initiate chemotherapy.

Most common cancer-related PIM drugs to be avoided

The monthly prevalence of cancer-related PIM use is presented in Figure 3a–c. Across all three cancer cohorts, the prevalence of amitriptyline use (a tricyclic antidepressant) was high, but remained relatively constant over the study period at 1.5–2.5%. The monthly prevalence of cyclobenzaprine (a muscle relaxant) was also steady, but lower across cohorts ranging from 0.5–1.5%. The lowest cancer-related PIM prevalence was for dicyclomine (an antispasmodic), which was also stable across the trajectory of care, with the exception of the colon cancer cohort, where a small spike in the month of diagnosis was observed.

For breast cancer, promethazine (an anti-emetic) was the most common cancer-related PIM, with a monthly prevalence that was elevated in the first nine months following cancer diagnosis (1%–3%), but returned to pre-diagnosis levels (<1%) thereafter. In the lung cancer cohort, the prevalence of promethazine and megestrol (a drug indicated to increase appetite) use increased after cancer diagnosis and remained elevated throughout the following year (promethazine: 1–3%; megestrol: 2–4%). The colon cancer cohort had the most cancer-related PIM use, including a high prevalence of metoclopramide, a pro-motility drug used to speed transit after surgery, (3–4%) and promethazine (3%) use during the initial months following diagnosis. Increasing prevalence in belladonna alkaloid use, an antispasmodic, (2–3%) and megestrol (1–3%) were largely sustained during the year following cancer diagnosis.

Period prevalence of potential drug-chemotherapeutic interactions

The 12-month period prevalence for selected potential drug-chemotherapeutic interactions are presented in Table 2 along with a brief description of the potential interaction outcome (e.g., increased chemotherapy effect). Overall, the reported period prevalence of potential drug-chemotherapy interactions ranged from 1–31%. The most prevalent potential interactions in the colon cancer cohort were for 5-FU/capecitabine and hydrochlorothiazide (a diuretic used to manage blood pressure, 22%) and warfarin (a drug used to treat blood clots, 15%), both classified as moderate potential drug interactions. In the breast cancer cohort, the most prevalent potential interactions classified as major included cyclophosphamide and hydrochlorothiazide (31%) and methotrexate and non-steroidal anti-inflammatory drugs (drugs used to inflammation, pain, and fever, 16%), while the most prevalent moderate interaction was for methotrexate in combination with proton-pump inhibitors (drugs used for suppression of gastric acid, 29%). Finally, in the lung cancer cohort, warfarin was considered a major interaction when used together with etoposide (14%) and gemcitabine (15%).

Discussion

Prior to cancer diagnosis, we observed that the vast majority of cancer patients used multiple prescription medications, many of which were considered to be potentially inappropriate according to the Beers criteria. However, following a cancer diagnosis, clear evidence of changes in patterns of medication use emerged, many as a direct result of cancer-related care. The prevalence of PIM dispensing increased following a diagnosis of colon and lung cancer, but decreased following a breast cancer diagnosis. When further stratified by chemotherapy receipt, changes in PIM prevalence were observed among those initiating chemotherapy in all cohorts. Further exploration of cancer-related PIM dispensing revealed that changes in PIM use were largely due to the addition of supportive care medications, in particular, anti-emetics and antispasmodic drugs. In addition, we observed a range of prevalence of potential drug-chemotherapy interactions across cohorts, with the most prevalent interactions involving hydrochlorothiazide, warfarin, and proton-pump inhibitors.

While a handful of studies have evaluated the prevalence of PIM use in older cancer patients at diagnosis or before initiating treatment,(30–34) only two prior studies have specifically used the 2012 Beers criteria to assess PIM prevalence. The first study by Maggiore et al(32) included 500 older adults with cancer initiating chemotherapy at seven academic medical centers in the United States. In this study, PIM prevalence, assessed via self-report and medical record verification, was 29%. This estimate is lower than that reported in our study, which may be due to the inclusion of: (1) only the Beers drugs to be avoided and not PIM drug-disease interactions and (2) individuals who were initiating chemotherapy. When restricted to older adults initiating chemotherapy, the PIM prevalence in our cohorts (prior to diagnosis) was lower (32–35%), likely because these populations are healthier and have a lower overall medication burden. The second study by Nightingale et al(33) was a conducted among 248 patients who underwent a routine comprehensive geriatric assessment at an academic medical center and had generally not received any cancer treatment or supportive care. PIM was assessed through a pharmacist-led medication review with the patient and/or

caregiver. The findings from this study are largely consistent with our results with a reported prevalence of PIM use (prior to cancer treatment) of 40%. Notably, neither of these studies evaluated patterns of PIM use over the trajectory of cancer care nor focused specifically on cancer-related PIM use. This information is important to clarify the unique medication-related issues facing older adults newly diagnosed with cancer and their healthcare providers.

It is important to recognize that the classification of a prescription drug as a PIM or cancer-related PIM only indicates that it might be inappropriate based on population-level data. There may be very good reasons for prescribing a medicine included on the Beers list, once the actual risks and benefits are considered within in the context of a particular individual and their cancer. Our findings indicate that changes in the prevalence of PIM dispensing over the course of cancer care are primarily driven by the use of supportive care medications among patients initiating chemotherapy. While some of these medications may not be considered inappropriate when administered in the oncology setting because of a lack of alternatives with fewer adverse effects (e.g., megestrol for appetite stimulation), others (e.g., metoclopramide or promethazine) have therapeutic alternatives with better benefit-risk profiles for older adult populations. If a PIM is used for treating an older adult with cancer, increased efforts to monitor and manage side effects may be warranted.

Only a handful of small studies have investigated the frequency of potential drug-drug interactions involving chemotherapies in cancer patients, and have found that drug interactions involving warfarin, quinolones, and antiepileptics are common,(23–28) consistent with our findings. Yet, no study evaluated the prevalence of these interactions among groups of older cancer patients truly at risk of an interaction (i.e., using a denominator of those patients receiving specific chemotherapies of interest). Thus, the estimates provided in this study fill an important gap clarifying the potential burden of these specific medication-related problems for cancer patients receiving chemotherapy. Still, caution is warranted when interpreting the potential drug-chemotherapy interaction analyses. Careful weighing of risks and benefits of specific medications in the context of a new cancer diagnosis and the expected benefits of cancer-directed treatment make these decisions particularly complex. In general, the severity of the potential drug-chemotherapy interaction may help to guide the level of concern and intervention or consultation with a pharmacy specialist.

We wholeheartedly concur with Nightingale and colleagues(33) that clinical pharmacists or pharmacologists can and should play a more prominent role in multidisciplinary teams caring for older adults with cancer. Pharmacy specialists are uniquely positioned to assess, plan, and optimize both oncology and non-oncology medications prior to beginning new cancer or supportive care treatments, as well as following the completion of cancer treatment by ensuring continuity and coordination of care with patients' general practitioner and medical specialists. This broader review of medication quality and safety for older adults can ultimately lead to improved cancer- and non-cancer outcomes. We found that the burden of PIM use varied by cancer site and chemotherapy receipt. Given resource constraints in busy oncology clinics, focused medication reviews, led by a pharmacy specialist, might target populations with the highest likelihood of being exposed to a medication-related problem. In

this study, we found that changes in PIM prevalence were largely driven by the receipt of chemotherapy. Taken together with concerns about the potential for drug interactions with specific chemotherapeutic agents, this population might be a reasonable target for more in-depth intervention via medication reviews.

The primary strengths of this study include the large, diverse study population of older breast, colon, and lung cancer patients treated in real world settings, expanding upon the generalizability of prior studies focused on patients treated in academic medical centers. In addition, our work provides an expanded view of PIM use by describing longitudinal patterns of PIM prevalence over the course of the cancer care continuum, highlighting subgroups and time points where PIM prevalence is increased. This analysis used prescription medication dispensing information to identify PIM, and thus captures a more complete assessment of prescription medications dispensed across various healthcare settings and providers, which is not subject to recall bias.

Our study is subject to some important limitations. Medicare claims data do not contain information on over-the-counter medications, herbal/supplements, or benzodiazepines (as they were not reimbursed by Medicare until 2013).(35) As such, the monthly PIM prevalence presented are likely underestimated, especially among patients initiating chemotherapy, where benzodiazepine prescribing is common.(36, 37) In addition, we did not attempt to identify all potential drug-chemotherapy interactions in our study cohort, but instead selected potential interactions for examination based on a literature review, indicating the most prevalent interactions. Finally, we did not evaluate specific outcomes of PIM dispensing or potential drug-chemotherapy interactions in older cancer patients (e.g., hospitalization, emergency department visits, mortality), however, we recognize this is an important area of future research.

Despite these limitations, this study has expanded our knowledge regarding potential medication-related problems among older adults newly diagnosed with breast, colon, and lung cancer over the course of cancer care. Our findings highlight the use of multiple supportive care medications and drug-interactions that may be considered potentially inappropriate among older cancer patients receiving chemotherapy. Physician assessment of medication risks and benefits and consideration of possible treatment alternatives seems reasonable, given the potentially adverse profile of these mediations in older adult populations. Given the unique and complex aspects of cancer-directed treatment and medication management among older adults newly diagnosed with cancer, inclusion of clinical pharmacists or pharmacologists on multidisciplinary teams caring for older cancer patients is warranted.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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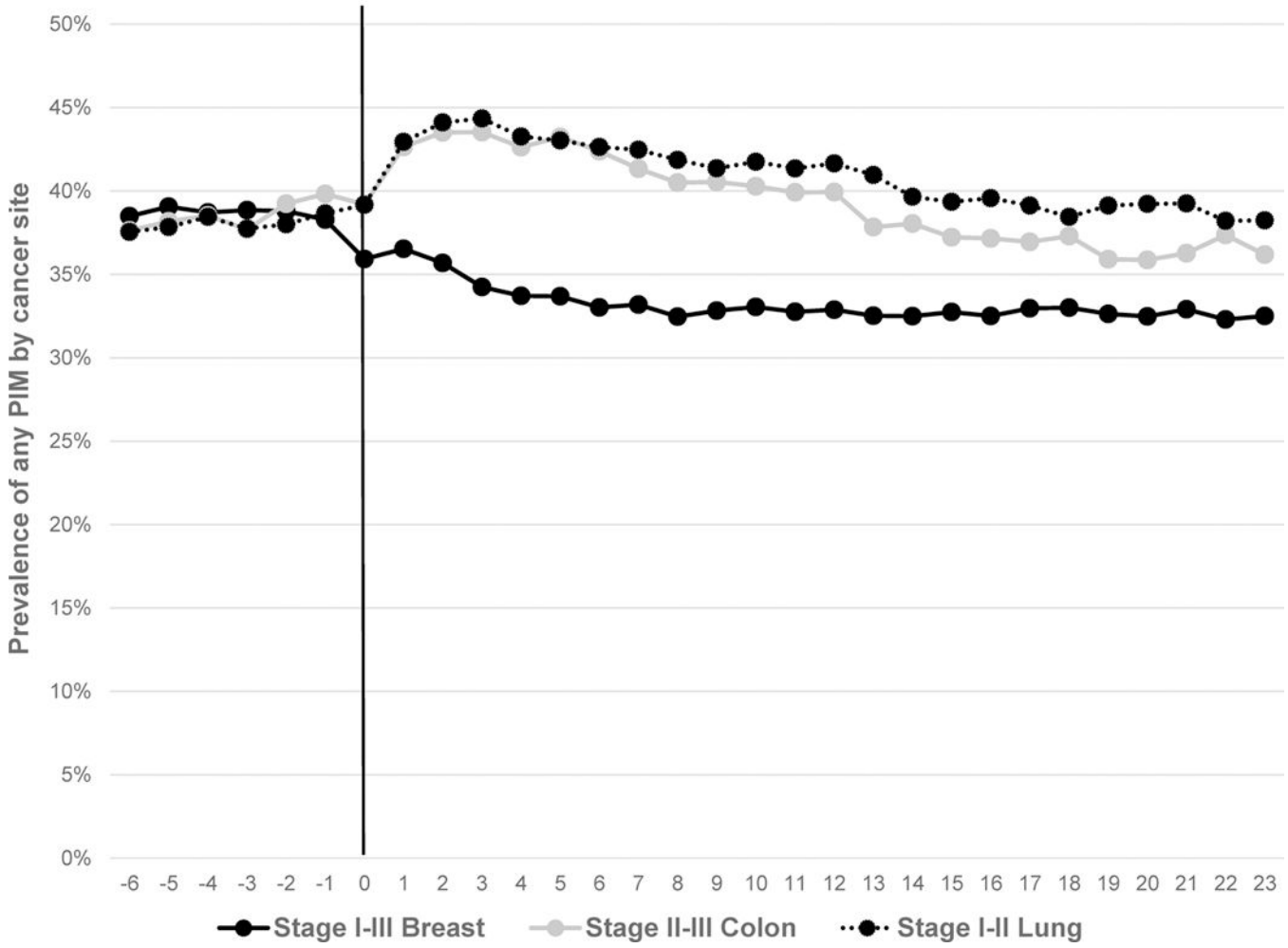

Figure 1. Monthly prevalence of any PIM by cancer site from 6 months before through 23 months following the month of cancer diagnosis

The solid black line represents the stage I–III breast cancer cohort; the solid grey line represents the stage II–III colon cancer cohort; the dashed black line represents the stage I–II lung cancer cohort. The black vertical line denotes the month of cancer diagnosis.

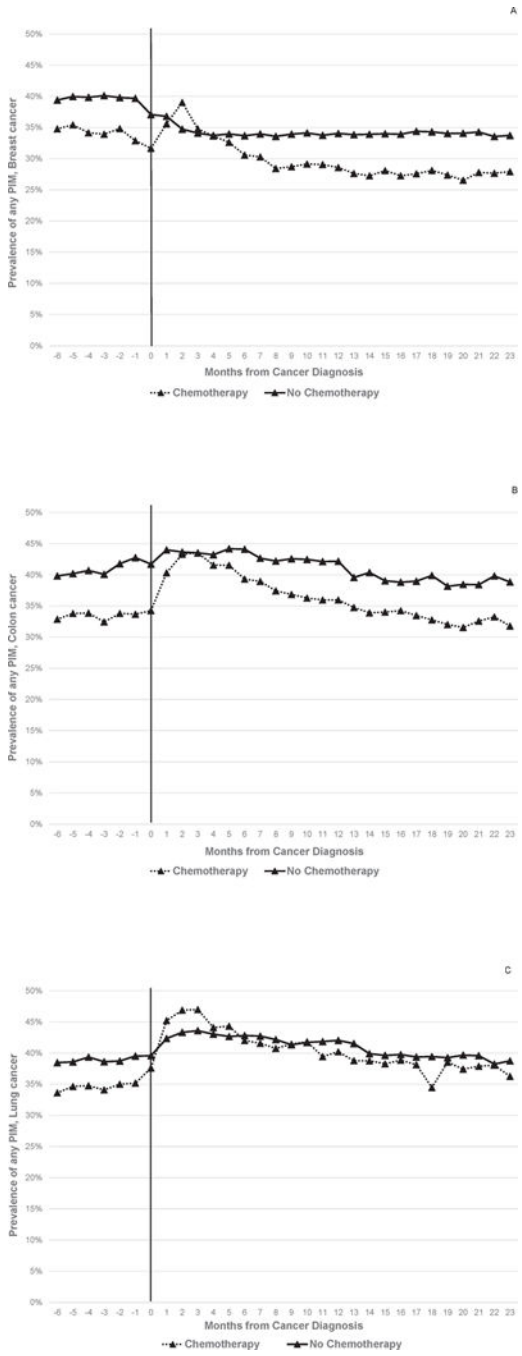

Figure 2. A–C. Monthly prevalence of PIM by cancer site from 6 months before through 23 months following the month of cancer diagnosis, stratified by chemotherapy receipt (dashed line) versus no chemotherapy receipt (solid line)

Chemotherapy initiation was assessed during the 6 months following cancer diagnosis. The black vertical line denotes the month of cancer diagnosis. Monthly PIM prevalence is reported by cancer site for the breast (A), colon (B), and lung (C) cohorts.

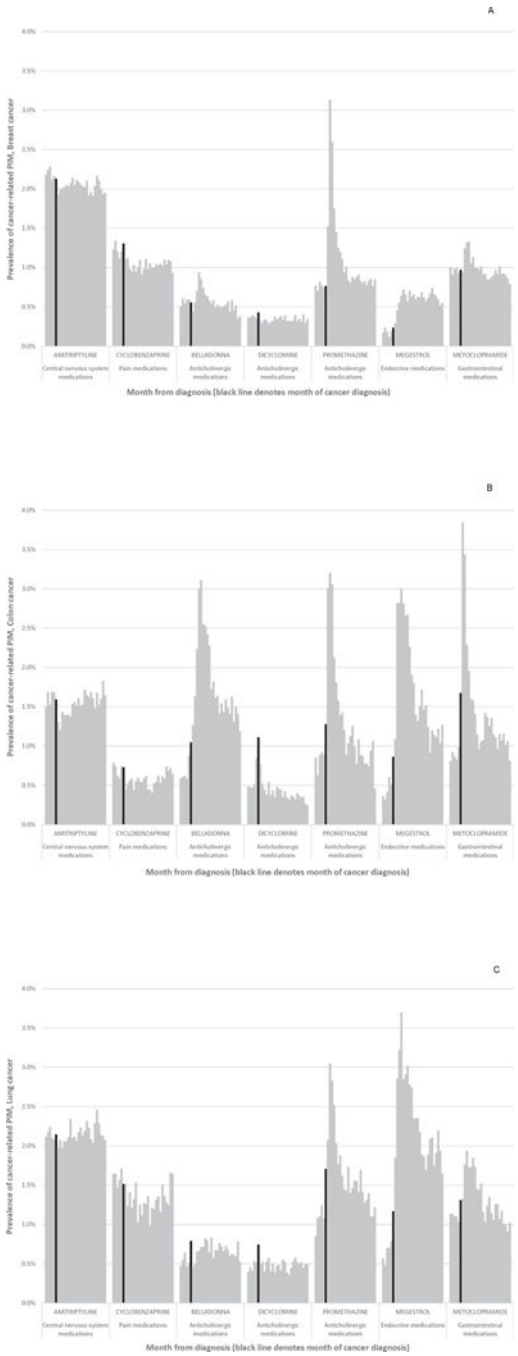

Figure 3. A–C. Monthly prevalence of cancer-related PIM from 6 months before through 23 months following the month of cancer diagnosis by cancer site

All medications included in the analysis had a prevalence of >1% in at least one month for at least one cancer site. The black vertical line denotes the month of cancer diagnosis. Monthly cancer-related PIM prevalence is reported by cancer site for the breast (A), colon (B), and lung (C) cohorts.

Table 1

Characteristics of patients at diagnosis by cancer site

Characteristic	Breast		Colon		Lung	
	N=19,318	%	N=7,283	%	N=7,237	%
Age at cancer diagnosis (years)						
66–69	4,319	22	1,083	15	1,571	22
70–74	4,845	25	1,555	21	1,981	27
75–79	4,207	22	1,543	21	1,755	24
80–84	3,253	17	1,504	21	1,247	17
85+	2,694	14	1,598	22	683	9
AJCC stage						
I	10,552	55	–	–	6,048	84
II	6,693	35	3,934	54	1,189	16
III	2,073	11	3,349	46	–	–
Sex						
Female	19,318	100	4,507	62	4,163	58
Race						
White	16,230	84	5,865	81	6,134	85
Black	1,682	9	638	9	572	8
Other	1,406	7	780	11	531	7
Marital status						
Married	7,655	40	3,128	43	3,367	47
Single	1,842	10	775	11	667	9
Other	9,821	51	3,380	46	3,203	44
Partnered/Unmarried	7,660	40	3,130	43	3,368	47
Divorced/Separated/Widowed	11,658	60	4,153	57	3,869	54
Year of cancer diagnosis						
2007	3,909	20	1,571	22	1,394	19
2008	3,826	20	1,518	21	1,481	21
2009	3,901	20	1,465	20	1,479	20
2010	3,799	20	1,363	19	1,463	20

Cancer Epidemiol Biomarkers Prev. Author manuscript; available in PMC 2019 January 01.

Characteristic	Breast		Colon		Lung	
	N=19,318	**%**	**N=7,283**	**%**	**N=7,237**	**%**
2011	3,883	20	1,366	19	1,420	20
Charlson comorbidity score						
0	10,572	55	3,434	47	2,291	32
1	5,076	26	1,995	27	2,343	32
2+	3,670	19	1,854	26	2,603	36
Predicted probability of frailty						
0–<10%	12,905	67	4,305	59	4,458	62
10–<20%	2,977	15	1,244	17	1,164	16
20–<50%	2,110	11	1,007	14	1,021	14
50%+	1,326	7	727	10	594	8
Number of prescription fills						
0–2	6,660	34	2,244	31	1,992	27
3–5	7,727	40	2,899	40	2,835	39
6–10	4,201	22	1,834	25	1,927	27
11+	731	4	306	4	483	7
Chemotherapy receipt	4,130	21	2,453	34	1,460	20
Surgical resection	18,090	94	7,147	98	3,350	46
Radiation receipt	8,581	44	135	2	2,129	29

Abbreviations: AJCC=American Joint Commission on Cancer

Table 2

The 12-month period prevalence of potential drug interactions with specified chemotherapeutics by cancer site

Site	Therapy (n)	Potential Drug Interaction	Interaction Outcomes	Ref	Severity	Exposed	Period Prevalence
Colon	5-FU/capecitabine (n=2199)	Hydrochlorothiazide	Increased myelosuppression due to thiazides	28	Moderate	490	22%
		Warfarin	Increased anticoagulant effect	13	Moderate	338	15%
		Phenytoin	Increased phenytoin effect	13	Moderate	25	1%
Breast	Cyclophosphamide (n=2796)	Hydrochlorothiazide	Increased myelosuppression due to thiazides	28	Major	856	31%
		Warfarin	Increased anticoagulant effect	24	Major	240	9%
		Allopurinol	Increased bone marrow suppression and toxicity	28	Major	63	2%
		Phenytoin	Increased phenytoin effect	28	Major	13	0.5%
		Fluconazole	Increased cyclophosphamide effect	24	Moderate	87	3%
		Digoxin	Reduced digoxin effect	24	Moderate	67	2%
		Quinolones	Reduced quinolone effect	26	Moderate	18	1%
	Doxorubicin (n=1224)	Quinolones	Reduced quinolone effect	28	Major	18	1%
		Digoxin	Reduced digoxin effect	24	Mild	23	2%
	Methotrexate (n=255)	NSAIDs	Reduced methotrexate clearance, increased effect	13	Major	42	16%
		Ciprofloxacin	Increased methotrexate effect	*a*	Moderate	22	9%
		PPIs	Increased methotrexate effect	29	Mild	74	29%
	Paclitaxel (n=1016)	Warfarin	Increased anticoagulant effect	13	Mild	109	11%
	Tamoxifen (n=2304)[b]	Warfarin	Increased anticoagulant effect	13	Major	206	9%
		Fluoxetine	Reduced anticancer effect of tamoxifen	13	Major	36	2%
		Paroxetine	Reduced anticancer effect of tamoxifen	13	Major	53	2%
Lung	Carboplatin (n=936)	Warfarin	Increased anticoagulant effect	13	Major	115	12%
		Phenytoin	Decreased phenytoin effect	24	Moderate	12	1%
		Quinolones	Reduced quinolone effect	28	Mild	18	2%
	Cisplatin (n=302)	Furosemide	Increased ototoxicity, unknown origin	24	Major	34	11%
	Etoposide (n=223)	Warfarin	Increased anticoagulant effect	13	Major	31	14%
	Gemcitabine (n=176)	Warfarin	Increased anticoagulant effect	13	Major	27	15%
	Paclitaxel (n=550)	Warfarin	Increased anticoagulant effect	13	Mild	70	13%

Abbreviations: NSAIDs = Non-steroidal anti-inflammatory drugs, PPIs=proton-pump inhibitors

[a]Identified by clinical pharmacist upon review.

[b] Included in analysis, although tamoxifen is considered an endocrine therapy.